

Claims

1. A substantially pure nucleic acid encoding a LIN-8 polypeptide, wherein said LIN-8 polypeptide comprises at least 130 contiguous amino acids of SEQ ID NO:1 and modulates cell proliferation.

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2. The nucleic acid of claim 1, wherein the amino acid sequence of said LIN-8 polypeptide comprises SEQ ID NO:1.

3. The nucleic acid of claim 1, wherein said LIN-8 polypeptide has an amino acid alteration relative to the sequence of SEQ ID NO:1.

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4. The nucleic acid of claim 3, wherein said LIN-8 polypeptide increases cell proliferation.

5. The nucleic acid of claim 1, wherein the polynucleotide sequence of said nucleic acid comprises SEQ ID NO:2.

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6. The nucleic acid of claim 1, wherein the polynucleotide sequence of said nucleic acid comprises at least 400 contiguous nucleotides of SEQ ID NO:2.

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7. The nucleic acid of claim 6, wherein said polynucleotide sequence of said nucleic acid comprises a mutant *lin-8* nucleic acid sequence.

8. The nucleic acid of claim 7, wherein said polynucleotide sequence comprises any one of SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, or SEQ ID NO:46.

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9. A mutant *lin-8* nucleic acid having a polynucleotide sequence comprising SEQ ID NO:20.

5 10. A mutant *lin-8* nucleic acid having a polynucleotide sequence comprising SEQ ID NO:22.

10 11. A polypeptide having an amino acid sequence identical to any one of SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, or SEQ ID NO:47.

15 12. A substantially pure nucleic acid encoding a LIN-56 polypeptide, wherein said LIN-56 polypeptide comprises at least 110 contiguous amino acids of SEQ ID NO:3 and modulates cell proliferation.

13. The nucleic acid of claim 12, wherein the amino acid sequence of said LIN-56 polypeptide comprises SEQ ID NO:3.

20 14. The nucleic acid of claim 12, wherein said LIN-56 polypeptide has an amino acid alteration relative to the sequence of SEQ ID NO:3.

15. The nucleic acid of claim 14, wherein said LIN-56 polypeptide increases cell proliferation.

25 16. The nucleic acid of claim 12, wherein the polynucleotide sequence of said nucleic acid comprises SEQ ID NO:4.

17. The nucleic acid of claim 12, wherein the polynucleotide sequence of said nucleic acid comprises at least 400 contiguous nucleotides of SEQ ID NO:4.

5 18. The nucleic acid of claim 17, wherein said polynucleotide sequence of said nucleic acid comprises a mutant *lin-56* nucleic acid sequence.

19. The nucleic acid of claim 18, wherein said polynucleotide sequence comprises SEQ ID NO:48.

10 20. A substantially pure nucleic acid encoding a LIN-61 polypeptide, wherein said LIN-61 polypeptide comprises at least 130 contiguous amino acids of SEQ ID NO:5 and modulates cell proliferation.

15 21. The nucleic acid of claim 20, wherein the amino acid sequence of said LIN-61 polypeptide comprises SEQ ID NO:5.

22. The nucleic acid of claim 20, wherein said LIN-61 polypeptide has an amino acid alteration relative to the sequence of SEQ ID NO:5.

20 23. The nucleic acid of claim 22, wherein said LIN-61 polypeptide increases cell proliferation.

24. The nucleic acid of claim 20, wherein the polynucleotide sequence of said nucleic acid comprises SEQ ID NO:6.

25 25. The nucleic acid of claim 20, wherein the polynucleotide sequence of said nucleic acid comprises at least 400 contiguous nucleotides of SEQ ID NO:6.

26. The nucleic acid of claim 25, wherein said polynucleotide sequence of said nucleic acid comprises a mutant *lin-61* nucleic acid sequence.

27. The nucleic acid of claim 26, wherein said polynucleotide sequence comprises any one of SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, or SEQ ID NO:78.

28. A polypeptide having an amino acid sequence identical to any one of SEQ ID NO:70, SEQ ID NO:71, or SEQ ID NO:72.

29. A vector comprising a nucleic acid having a polynucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:73, SEQ ID NO:74, and SEQ ID NO:75.

30. A transgenic cell comprising a nucleic acid sequence encoding a *lin-8*, a *lin-56*, or a *lin-61* polypeptide, wherein said nucleic acid sequence is located in the genome of said cell in a position in which it does not naturally occur.

31. The method of claim 30, wherein said nucleic acid sequence is operably linked to a heterologous promoter.

32. A purified antibody which specifically binds to a LIN-8 polypeptide.

33. A purified antibody which specifically binds to a LIN-56 polypeptide.

34. A purified antibody which specifically binds to a LIN-61 polypeptide.

35. A method of modulating proliferation of a cell, said method comprising administering to said cell a proliferation-modulating amount of a polypeptide having the amino acid sequence of SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5.

36. The method of claim 35, wherein said cell is in a mammal.

37. The method of claim 36, wherein said mammal is a human.

38. A method of modulating proliferation of a cell, said method comprising administering to said cell a proliferation-modulating amount of a nucleic acid sequence encoding a polypeptide having the amino acid sequence of any one of SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5.

39. The method of claim 38, wherein said nucleic acid sequence is contained in a vector.

40. A method of identifying a compound that modulates cell proliferation, said method comprising:

(a) providing a cell expressing a nucleic acid operably linked to a *lin-8*, *lin-56*, or *lin-61* promoter;

(b) contacting said cell with a candidate compound; and

(c) measuring the expression of said nucleic acid, wherein an alteration in the level of expression of said nucleic acid indicates the presence of a compound that modulates cell proliferation.

41. The method of claim 40, wherein said nucleic acid is selected from the group consisting of *lin-8*, *lin-56*, and *lin-61*.

42. The method of claim 40, wherein said nucleic acid is a reporter gene.

43. The method of claim 40, wherein step (c) comprises measuring the expression of the protein encoded by said nucleic acid.

44. The method of claim 43, wherein said protein is contacted with an antibody that specifically binds to a LIN-8, LIN-56, or LIN-61 polypeptide.

45. The method of claim 40, wherein step (c) comprises measuring the mRNA level of said nucleic acid.

46. A method of identifying a candidate compound that binds to a LIN-8, LIN-56, or LIN-61 polypeptide, said method comprising:

- (a) providing said polypeptide;
- (b) contacting said polypeptide with a candidate compound; and
- (c) measuring the binding of said candidate compound to said polypeptide, said binding indicating the presence of a candidate compound that binds a LIN-8, LIN-56, or LIN-61 polypeptide.

47. The method of claim 46, wherein said candidate compound is a polypeptide.

48. A method of diagnosing an animal for the presence of a cell proliferation disease, or an increased likelihood of developing a cell proliferation disease, said method comprising, determining whether a nucleic acid sample obtained from said animal comprises a mutant *lin-8*, *lin-56*, or *lin-61* nucleic acid, wherein the presence of said

mutant *lin-8*, *lin-56*, or *lin-61* nucleic acid indicates that said animal has a cell proliferation disease, or is at an increased likelihood of developing a cell proliferation disease.

5 49. The method of claim 48, wherein said mutant *lin-8* nucleic acid is selected from the group consisting of *lin-8(n2738)*, *lin-8(n2731)*, *lin-8(n3606)*, *lin-8(n3595)*, *lin-8(n2739)*, *lin-8(n3586)*, *lin-8(n3588)*, *lin-8(n111)*, *lin-8(n2741)*, *lin-8(n3585)*, *lin-8(n3646)*, *lin-8(n2376)*, *lin-8(n2378)*, *lin-8(n2403)*, *lin-8(n2724)*, *lin-8(n3607)*, *lin-8(n3591)*, *lin-8(n3609)*, and *lin-8(n3581)*.

10 50. The method of claim 48, wherein said mutant *lin-56* nucleic acid is a *lin-56(n3355)* or *lin-56(n2728)* nucleic acid.

15 51. The method of claim 48, wherein said mutant *lin-61* nucleic acid is selected from the group consisting of *lin-61(n3446)*, *lin-61(n3447)*, *lin-61(n3624)*, and *lin-61(n3635)*.

20 52. The method of claim 48, wherein said cell proliferation disease is cancer.

25 53. A method of diagnosing an animal for the presence of a cell proliferation disease, or an increased likelihood of developing a cell proliferation disease, said method comprising measuring *lin-8*, *lin-56*, or *lin-61* nucleic acid expression in a sample obtained from said animal, wherein an alteration in said expression, relative to a sample obtained from an unaffected animal, indicates that said animal has a cell proliferation disease, or an increased likelihood of developing a cell proliferation disease.

 54. The method of claim 53, wherein said nucleic acid expression is measured by measuring the amount of said LIN-8, LIN-56, or LIN-61 polypeptide in said sample.

55. The method of claim 54, wherein said amount of said LIN-8, LIN-56, or LIN-61 polypeptide is measured using an antibody that specifically binds to a LIN-8, LIN-56, or LIN-61 polypeptide.

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56. The method of claim 53, wherein said nucleic acid expression is measured by measuring the amount of *lin-8*, *lin-56*, or *lin-61* mRNA in said sample.

57. The method of claim 53, wherein said animal is a mammal.

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58. The method of claim 57, wherein said mammal is a human.

59. A method of identifying a nucleic acid that modulates cell proliferation, said method comprising:

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(a) expressing in a cell (i) a first nucleic acid operably linked to a first promoter, wherein said first promoter is selected from the group consisting of the *lin-8*, *lin-56*, and *lin-61* promoter; and (ii) a second nucleic acid operably linked to a second promoter; and

(b) measuring the expression of said first nucleic acid, wherein a modulation in said expression of said first nucleic acid in the presence of said second nucleic acid, indicates that said second nucleic acid modulates cell proliferation.

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60. The method of claim 59, wherein said first nucleic acid is selected from the group consisting of a *lin-8*, *lin-56*, and *lin-61* nucleic acid.

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